ATTACHMENT A

Clean Replacement Paragraphs

At the following locations, replace the previously provided paragraph with the following clean paragraph(s).

Page 1, lines 3-5.

This is a 371 of PCT/FR98/00328 filed February 19, 1998.

B1

FIELD OF THE INVENTION

The invention relates to the use of proteins designed ULIP/POP in the diagnosis and therapy of cancers and paraneoplastic neurological syndromes.

BACKGROUND OF THE INVENTION

Page 5, after line 2 insert the heading

B2

SUMMARY OF THE INVENTION

Page 16, line 1

B3

DESCRIPTION OF THE DRAWINGS

Page 18, lines 31-35

B4

The amino acid sequence has been completed in SEQ ID No. 8 by 19 C-terminal amino acids (No. 554 to No. 568). This C-terminal region which is missing in Figure 12 is very well conserved between rat and mice ULIP-4 as well as between the different ULIPs.

Page 19, before line 1 insert

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

B5

The present invention will be described with reference to the following examples.

Pages 45-59

Please replace the Sequence Listing with the enclosed substitute Sequence Listing provided herewith as **Attachment C**.

clean paragraphs

ATTACHMENT B

Marked Up Replacement Paragraphs

At the following locations, a marked up copy of the replaced paragraph is provided.

Page 1, lines 3-5.

This is a 371 of PCT/FR98/00328 filed February 19, 1998.

FIELD OF THE INVENTION

The invention relates to the use of proteins designed ULIP/POP in the diagnosis and therapy of cancers and paraneoplastic neurological syndromes.

BACKGROUND OF THE INVENTION

Page 5, after line 2 insert the heading

SUMMARY OF THE INVENTION

Page 16, line 1

~~LEGEND TO THE FIGURES~~ DESCRIPTION OF THE DRAWINGS

Page 18, lines 31-35

The amino acid sequence has been completed in SEQ ID No. 8 by ~~15~~ 19 C-terminal amino acids (No. 554 to No. 568). This C-terminal region which is missing in Figure 12 is very well conserved between rat and mice ULIP-4 as well as between the different ULIPs.

Page 19, before line 1 insert

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The present invention will be described with reference to the following examples.

Pages 45-59

Please replace the Sequence Listing with the enclosed substitute Sequence Listing provided herewith as **Attachment C**.

marked paragraphs

ATTACHMENT C

Substitute Sequence Listing

clean paragraphs

ATTACHMENT D

Clean Replacement/New Claims (entire set of pending claims)

Following herewith is a clean copy of the entire set of pending claims.

1. (Amended) A purified ULIP polypeptide comprising an amino acid sequence selected from SEQ ID No. 2, No. 4, No. 6 and No. 8.

2. (Amended) The purified ULIP polypeptide according to Claim 1, comprising the amino acid sequence SEQ ID No. 8.

3. (Amended) An isolated nucleotide acid comprising a sequence coding for a ULIP polypeptide of amino acid sequence SEQ ID No. 2, No. 4, No. 6 or No. 8.

4. (Amended) The nucleic acid according to Claim 3, comprising a sequence selected from SEQ ID No. 1, No. 3, No. 5 or No. 7, respectively coding the ULIP polypeptide of amino acid sequence SEQ ID No. 2, No. 4, No. 6 or No. 8.

5. (Twice Amended) The nucleic acid according to Claim 4, comprising the nucleotide sequence SEQ ID No. 7 coding the amino acid sequence SEQ ID No. 8.

6. (Twice Amended) A cloning and/or expression vector containing a nucleic acid sequence according to Claim 3.

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7. (Amended) A host cell transfected by a vector according to Claim 6.

9. (Amended) A composition useful for the diagnosis of paraneoplastic neurological syndromes and/or for the early diagnosis of the formation of tumors, said composition comprising a purified polypeptide comprising amino acid sequence SEQ ID No. 8.

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10. (Twice Amended) A method for using purified ULIP polypeptide comprising SEQ ID No. 8, a derivative or biologically active polypeptide fragment thereof, or of a nucleic acid comprising the nucleotide sequence of SEQ ID No. 7 for detecting the presence of anti-CV2 antibodies in a biological sample.

14. (Amended) A method for the diagnosis of paraneoplastic neurological syndromes and/or for the early diagnosis of the formation of tumors, comprising:

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- contacting a blood sample taken from an individual with a purified ULIP polypeptide, comprising SEQ ID No. 8, a derivative or biologically active polypeptide fragment thereof, optionally attached to a support under conditions allowing the formation of specific immunological complexes between the polypeptide and the auto-antibodies optionally present in the blood sample, and
- detecting specific immunological complexes optionally formed, the specific immunological complexes being indicative of a paraneoplastic neurological syndrome or of a tumor.

clean claims

15. (Amended) A kit for diagnosis in paraneoplastic neurological syndromes and for deleting early diagnosis of the formation of tumors from a biological sample, comprising:

B8

- at least one purified ULIP polypeptide comprising SEQ ID No. 8, a derivative or biologically active polypeptide fragment of the ULIP optionally attached to a support, and

- means of visualization of the formation of specific antigen/antibody complexes between an anti-POP-66 auto-antibody and the purified ULIP polypeptide, derivative or polypeptide fragment and/or means of qualification of these complexes.

16. Canceled.

17. Canceled.

20. (Amended) A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising the steps of:

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contacting a sample from the subject with a polypeptide comprising a purified ULIP polypeptide selected from the group consisting of amino acid SEQ ID No. 8, a derivative or biological active polypeptide thereof, said contacting carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of a paraneoplastic syndrome in said subject.

clean claims

21. (Amended) The method of claim 20, wherein the polypeptide sequence is SEQ ID No. 8.

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22. (Amended) The method of claim 20, wherein the polypeptide is an antigenic fragment of a polypeptide comprising amino acid sequence SEQ ID No. 8.

23. A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising, the steps of:

contacting a sample from the subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a specific immunological complex with a ULIP polypeptide, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of a paraneoplastic syndrome in said subject.

24. (Amended) A method of diagnosing a paraneoplastic syndrome in a subject, said method comprising the steps of:

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contacting a sample from said subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a specific immunological complex with a polypeptide comprising amino acid sequence

SEQ ID No. 8, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed between the peptide and antibodies in the sample;

wherein the presence of specific immunological complexes formed between the peptide and antibodies is indicative of a paraneoplastic syndrome in said subject

B 10

25. (Amended) A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said subject with a polypeptide comprising amino acid sequence SEQ ID No. 8, said contacting carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of the formation of a tumor in said subject.

26. (Amended) The method of claim 25, wherein the polypeptide comprising amino acid sequence SEQ ID No. 8.

27. (Amended) The method of claim 25, wherein the polypeptide is an antigenic fragment of a polypeptide comprising amino acid sequence SEQ ID No. 8.

clean claims

28. A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said, subject with a ULIP polypeptide, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed;

wherein the presence of immunological complexes is indicative of the formation of a tumor in said subject.

B 10

29. (Amended) A method of diagnosing the formation of a tumor of cancerous origin in a subject, said method comprising the steps of:

contacting a sample from said subject with a peptide capable of forming a specific immunological complex with an antibody, said antibody capable of forming a specific immunological complex with a polypeptide comprising amino acid sequence SEQ ID No. 8, wherein said contacting is carried out under conditions sufficient to allow the formation of specific immunological complexes between the peptide and antibodies present within the sample; and

detecting the specific immunological complexes formed between the peptide and antibodies in the sample;

wherein the presence of specific immunological complexes formed between the peptide and antibodies is indicative of the formation of a tumor in said subject.

30. (Amended) A diagnostic substrate for *ex vivo* identifying antibodies to a polypeptide comprising amino acid sequence SEQ ID No. 8 in a subject, said substrate comprising:

a solid support; and

a peptide comprising an antigenic portion of said polypeptide.

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31. (Amended) The substrate of claim 30, wherein the support comprises animal brain, and wherein the antigenic portion of the polypeptide is endogenous to said brain.

C3

32. (Amended) The substrate of claim 30, wherein the antigenic portion of a polypeptide comprising amino acid sequence of SEQ ID No. 8 is attached to said support.

33. (Amended) A diagnostic kit for identifying antibodies to a polypeptide comprising amino acid sequence of SEQ ID No. 8 in a subject, said kit comprising an antigenic portion of said polypeptide or a derivative thereof.

34. (Amended) The kit of claim 33, wherein the kit further comprises means of visualizing formation of said polypeptide-antibody complexes.

35. (Amended) The kit of claim 33, wherein the antigenic portion of said polypeptide is purified.